FORM LG-4878

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E. I. DU PONT DE NEMOURS & COMPANY
INCORPORATED
WILMINGTON, DELAWARE 19898

LEGAL DEPARTMENT

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September 11, 1992

Document Processing Center (TS-790)
Office of Pollution Prevention and Toxics
Environmental Protection Agency
401 M Street., S.W.
Washington, D.C. 20460
Attn: Section 8(e) Coordinator (CAP Agreement)

88920010974

Dear Coordinator:

8ECAP-0025

On behalf of the Regulatee and pursuant to Unit II B.1.b. and Unit II C of the 6/28/91CAP Agreement, E.I. Du Pont de Nemours and Co. hereby submits (*in triplicate*) the attached studies. Submission of this information is voluntary and is occasioned by unilateral changes in EPA's standard as to what EPA now considers as reportable information. Regulatee's submission of information is made solely in response to the new EPA §8(e) reporting standards and is not an admission: (1) of TSCA violation or liability; (2) that Regulatee's activities with the study compounds reasonably support a conclusion of substantial health or environmental risk or (3) that the studies themselves reasonably support a conclusion of substantial health or environmental risk.

The "Reporting Guide" creates new TSCA 8(e) reporting criteria which were not previously announced by EPA in its 1978 Statement of Interpretation and Enforcement Policy, 43 Fed Reg 11110 (March 16, 1978). The "Reporting Guide states criteria which expands upon and conflicts with the 1978 Statement of Interpretation. Absent amendment of the Statement of Interpretation, the informal issuance of the "Reporting Guide" raises significant due processes issues and clouds the appropriate reporting standard by which regulated persons can assure TSCA Section 8(e) compliance.

For Regulatee,

ORIGINAL

8E CAP

Mark H. Christman
Counsel
Legal D-7158
1007 Market Street
Wilmington, DE 19898
(302) 774-6443

RECEIVED
3/24/95

ATTACHMENT 1

Submission of information is made under the 6/28/91 CAP Agreement, Unit II. This submission is made voluntarily and is occasioned by recent changes in EPA's TSCA §8(e) reporting standard; such changes made, for the first time in 1991 and 1992 without prior notice and in violation of Regulatee's constitutional due process rights. Regulatee's submission of information under this changed standard is not a waiver of its due process rights; an admission of TSCA violation or liability, or an admission that Regulatee's activities with the study compounds reasonably support a conclusion of substantial risk to health or to the environment. Regulatee has historically relied in good faith upon the 1978 Statement of Interpretation and Enforcement Policy criteria for determining whether study information is reportable under TSCA §8(e), 43 Fed Reg 11110 (March 16, 1978). EPA has not, to date, amended this Statement of Interpretation.

After CAP registration, EPA provided the Regulatee the June 1, 1991 "TSCA Section 8(e) Reporting Guide". This "Guide" has been further amended by EPA, EPA letter, April 10, 1992. EPA has not indicated that the "Reporting Guide" or the April 1992 amendment supersedes the 1978 Statement of Interpretation. The "Reporting Guide" and April 1992 amendment substantively lowers the Statement of Interpretation 's TSCA §8(e) reporting standard[2]. This is particularly troublesome as the "Reporting Guide" states criteria, applied retroactively, which expands upon and conflicts with the Statement of Interpretation.[3] Absent amendment of the Statement of Interpretation, the informal issuance of the "Reporting Guide" and the April 1992 amendment clouds the appropriate standard by which regulated persons must assess information for purposes of TSCA §8(e).

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[2]In sharp contrast to the Agency's 1977 and 1978 actions to soliciting public comment on the proposed and final §8(e) Policy, EPA has unilaterally pronounced §8(e) substantive reporting criteria in the 1991 Section 8(e) Guide without public notice and comment, See 42 Fed Reg 45362 (9/9/77), "Notification of Substantial Risk under Section 8(e): Proposed Guidance".

[3]A comparison of the 1978 Statement of Interpretation and the 1992 "Reporting Guide" is a appended.

Throughout the CAP, EPA has mischaracterized the 1991 guidance as reflecting "longstanding" EPA policy concerning the standards by which toxicity information should be reviewed for purposes of §8(e) compliance. Regulatee recognizes that experience with the 1978 Statement of Interpretation may cause a review of its criteri. Regulatee supports and has no objection to the Agency's amending reporting criteria *provided that* such amendment is not applied to the regulated community in an unfair way. However, with the unilateral announcement of the CAP under the auspices of an OCM enforcement proceeding, EPA has wrought a terrific unfairness since much of the criteria EPA has espoused in the June 1991 Reporting Guide and in the Agency's April 2, 1992 amendment is new criteria which does not.exist in the 1978 Statement of Interpretation and Enforcement Policy.

The following examples of new criteria contained in the "Reporting Guide" that is not contained in the Statement of Interpretation follow:

- o even though EPA expressly disclaims each "status report" as being preliminary evaluations that should not be regarded as final EPA policy or intent[4], the "Reporting Guide" gives the "status reports" great weight as "sound and adequate basis" from which to determine mandatory reporting obligations. ("Guide" at page 20).
- o the "Reporting Guide" contains a matrix that establishes new numerical reporting "cutoff" concentrations for acute lethality information ("Guide" at p. 31). Neither this matrix nor the cutoff values therein are contained in the Statement of Interpretation. The regulated community was not made aware of these cutoff values prior to issuance of the "Reporting Guide" in June, 1991.
- othe "Reporting Guide" states new specific definitional criteria with which the Agency, for the first time, defines as 'distinguishable neurotoxicological effects'; such criteria/guidance not expressed in the 1978 Statement of Interpretation.[5];

- othe "Reporting Guide" provides new review/ reporting criteria for irritation and sensitization studies; such criteria not previously found in the 1978 Statement of Interpretation/Enforcement Policy.
- othe "Reporting Guide" publicizes certain EPA Q/A criteria issued to the Monsanto Co. in 1989 which are not in the Statement of Interpretation; have never been published in the Federal Register or distributed by the EPA to the Regulatee. Such Q/A establishes new reporting criteria not previously found in the 1978 Statement of Interpretation/Enforcement Policy .

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[4]The 'status reports' address the significance, if any, of particular information reported to the Agency, rather than stating EPA's interpretation of §8(e) reporting criteria. In the infrequent instances in which the status reports contain discussion of reportability, the analysis is invariably quite limited, without substantial supporting scientific or legal rationale.

[5] *See, e.g,* 10/2/91 letter from Du Pont to EPA regarding the definition of 'serious and prolonged effects' as this term may relate to transient anesthetic effects observed at lethal levels; 10/1/91 letter from the American Petroleum Institute to EPA regarding clarification of the Reporting Guide criteria.

In discharging its responsibilities, an administrative agency must give the regulated community fair and adequate warning to as what constitutes noncompliance for which penalties may be assessed.

> Among the myriad applications of the due process clause is the fundamental principle that statutes and regulations which purport to govern conduct must give an adequate warning of what they command or forbid.... Even a regulation which governs purely economic or commercial activities, if its violation can engender penalties, must be so framed as to provide a constitutionally adequate warning to those whose activities are governed.

Diebold, Inc. v. Marshall, 585 F.2d 1327, 1335-36 (D.C. Cir. 1978). *See also*, Rollins Environemntal Services (NJ) Inc. v. U.S. Environmental Protection Agency, 937 F. 2d 649 (D.C. Cir. 1991).

While neither the are rules, This principle has been applied to hold that agency 'clarification', such as the Statement of Interpretation, the "Reporting Guide" nor the April 1992 amendments will not applied retroactively.

> ...a federal court will not retroactively apply an unforeseeable interpretation of an administrative regulation to the detriment of a regulated party on the theory that the post hoc interpretation asserted by the Agency is generally consistent with the policies underlying the Agency's regulatory program, when the semantic meaning of the regulations, as previously drafted and construed by the appropriate agency, does not support the interpretation which that agency urges upon the court.

Standard Oil Co. v. Federal Energy Administration, 453 F. Supp. 203, 240 (N.D. Ohio 1978), aff'd sub nom. Standard Oil Co. v. Department of Energy, 596 F.2d 1029 (Em. App. 1978):

The 1978 Statement of Interpretation does not provide adequate notice of, and indeed conflicts with, the Agency's current position at §8(e) requires reporting of all 'positive' toxicological findings without regard to an assessment of their relevance to human health. In accordance with the statute, EPA's 1978 Statement of Interpretation requires the regulated community to use scientific judgment to evaluate the significance of toxicological findings and to determining whether they reasonably support a conclusion of a substantial risk. Part V of the Statement of Interpretation urges persons to consider "the fact or probability" of an effect's occurrence. Similarly, the 1978 Statement of Interpretation stresses that an animal study is reportable only when "it contains reliable evidence ascribing the effect to the chemical." 43 Fed Reg. at 11112. Moreover, EPA's Statement of Interpretation defines the substantiality of risk as a function of both the seriousness of the effect and the probability of its occurrence. 43 Fed Reg 11110 (1978). Earlier Agency interpretation also emphasized the "substantial" nature of a §8(e) determination. See 42 Fed Reg 45362, 45363

(1977). [Section 8(e) findings require "extraordinary exposure to a chemical substance...which critically imperil human health or the environment"].

The recently issued "Reporting Guide" and April 1992 Amendment guidance requires reporting beyond and inconsistent with that required by the Statement of Interpretation. Given the statute and the Statement of Interpretation's explicit focus on substantial human or environmental risk, whether a substance poses a "substantial risk" of injury requires the application of scientific judgment to the available data on a case-by-case basis.

If an overall weight-of-evidence analysis indicates that this classification is unwarranted, reporting should be unnecessary under §8(e) because the available data will not "reasonably support the conclusion" that the chemical presents a substantial risk of serious adverse consequences to human health.

Neither the legislative history of §8(e) nor the plain meaning of the statute support EPA's recent lowering of the reporting threshold that TSCA §8(e) was intended to be a sweeping information gathering mechanism. In introducing the new version of the toxic substances legislation, Representative Eckhart included for the record discussion of the specific changes from the version of H. R. 10318 reported by the Consumer Protection and Finance Subcommittee in December 1975. One of these changes was to modify the standard for reporting under §8(e). The standard in the House version was changed from "causes or contributes to an unreasonable risk" to "causes or significantly contributes to a substantial risk". This particular change was one of several made in TSCA §8 to avoid placing an undue burden on the regulated community. The final changes to focus the scope of Section 8(e) were made in the version reported by the Conference Committee.

The word "substantial" means "considerable in importance, value, degree, amount or extent". Therefore, as generally understood, a "substantial risk" is one which will affect a considerable number of people or portion of the environment, will cause serious injury and is based on reasonably sound scientific analysis or data. Support for the interpretation can be found in a similar provision in the Consumer Product Safety Act. Section 15 of the CPSA defines a "substantial product hazard" to be:

> "a product defect which because of the pattern of defect, the number of defective products distributed in commerce, the severity of the risk, or otherwise, creates a substantial risk of injury to the public."

Similarly, EPA has interpreted the word 'substantial' as a quantitative measurement. Thus, a 'substantial risk' is a risk that can be quantified, *See,* 56 Fed Reg 32292, 32297 (7/15/91). Finally, since information pertinent to the exposure of humans or the environment to chemical substances or mixtures may be obtained by EPA through Sections 8(a) and 8(d) regardless of the degree of potential risk, §8(e) has specialized function. Consequently, information subject to §8(e) reporting should be of a type which would lead a reasonable man to conclude that some type action was required immediately to prevent injury to health or the environment.

Attachment

Comparison:

Reporting triggers found in the 1978 "Statement of Interpretation/ Enforcement Policy",43 Fed Reg 11110 (3/16/78) and the June 1991 *Section 8(e) Guide.*

TEST TYPE	1978 POLICY CRITERIA EXIST?	New 1991 GUIDE CRITERIA EXIST?
ACUTE LETHALITY		
Oral	N}	Y}
Dermal	N}	Y}
Inhalation (Vapors)	}[6]	}[7]
aerosol	N}	Y}
dusts/ particles	N}	Y}
SKIN IRRITATION	N	Y[8]
SKIN SENSITIZATION (ANIMALS)	N	Y[9]
EYE IRRITATION	N	Y[10]
SUBCHRONIC (ORAL/DERMAL/INHALATION)	N	Y[11]
REPRODUCTION STUDY	N	Y[12]
DEVELOPMENTAL TOX	Y[13]	Y[14]

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[6] 43 Fed Reg at 11114, comment 14:

"This policy statements directs the reporitng of specifiec effects when unknown to the Administrator. Many routine tests are based on a knowledge of toxicity associated with a chemicalL unknown effects occurring during such a range test may have to be reported if they are those of concern tot he Agency and if the information meets the criteria set forth in Parts V and VII."

[7] Guide at pp.22, 29-31.

[8] Guide at pp-34-36.

[9] Guide at pp-34-36.

[10] Guide at pp-34-36.

[11] Guide at pp-22; 36-37.

[12] Guide at pp-22

[13] 43 Fed Reg at 11112

"Birth Defects" listed.

[14] Guide at pp-22

NEUROTOXICITY	N	Y[15]
CARCINOGENICITY	Y[16]	Y[17]
MUTAGENICITY		
In Vitro	Y}[18]	Y} [19]
In Vivo	Y}	Y}
ENVIRONMENTAL		
Bioaccumulation	Y}	N
Bioconcentration	Y}[20]	N
Oct/water Part. Coeff.	Y}	N
Acute Fish	N	N
Acute Daphnia	N	N
Subchronic Fish	N	N
Subchronic Daphnia	N	N
Chronic Fish	N	N
AVIAN		
Acute	N	N
Reproductive	N	N
Reprodcutive	N	N

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[15] Guide at pp-23; 33-34.

[16] 43 Fed Reg at 11112
"Cancer" listed

[17] Guide at pp-21.

[18] 43 Fed Reg at 11112; 11115 at Comment 15
"Mutagenicity" listed/ *in vivo* vs *invitro* discussed; discussion of "Ames test".

[19] Guide at pp-23.

[20] 43 Fed Reg at 11112; 11115 at Comment 16.

CAS #19355-69-2
Chem: Propanenitrile, 2-amino-2-methyl-
Title: One-hour Inhalation Median Lethal Concentration LC50) Study of Vazo 64AN in Rats
Date: September 28, 1987
Summary of Effects: Fatal at 113 ppm+.

Study Title

One-hour Inhalation Median Lethal Concentration (LC50) Study of Vazo® 64AN in Rats

Author

Laura A. Kinney

Study Completed On

September 28, 1987

Performing Laboratory

E. I. du Pont de Nemours and Company, Inc.
Haskell Laboratory for Toxicology and Industrial Medicine
Elkton Road, P. O. Box 50
Newark, Delaware 19714

Medical Research No.

8165-001

Laboratory Project ID

Haskell Laboratory Report No. 535-87

GOOD LABORATORY PRACTICE COMPLIANCE STATEMENT

This study was conducted according to EPA Good Laboratory Practice Regulations (40 CFR 792). Any areas of noncompliance are documented in the study records. No deviations existed that significantly affected the validity of the study.

Submitter: E. I. du Pont de Nemours and Company, Inc.

Sponsor: Chemicals and Pigments Department
E. I. du Pont de Nemours and Company, Inc.

Study Director: Laura A. Kinney 9/22/87
Laura A. Kinney
Chemist
Acute and Developmental Toxicology Section

GENERAL INFORMATION (Con't)

Stability: The test material is known to decompose to form cyanohydrin salts and ammonia. Decomposition occurs over a period of weeks when the material is not stored under ammonia vapor, and can occur more quickly when exposed to heat. To avoid these problems, the test material was supplied under ammonia, and the minimum amount of heat needed to evaporate the aminonitrile was used in the generation system. Under these conditions, the test material was assumed to be stable.

In-Life Phase Initiated - Completed: 4/8/87 - 4/23/87

Notebook: E-51182, pp. 117-146.
E-51261, pp. 46-48.

Sponsor: Chemicals and Pigments Department
E. I. du Pont de Nemours and Company, Inc.
Wilmington, Delaware

Material Submitted by: Roland Kohl
W. R. Grace and Company
Organic Chemicals Division
55 Hayden Avenue
Lexington, Massachusetts 02173

There are 12 pages in this report.

Distribution:
K. D. Dastur (1)
J. C. Watts (1)
H. J. Trochimowicz (1)
N. C. Chromey/L.A. Kinney (1)
C. W. Hutt (1)

QUALITY ASSURANCE DOCUMENTATION

STUDY: MR 8165-001 One-hour Inhalation Median Lethal Concentration (LC50)
H# 16,716 Study of Vazo® 64AN in Rats

Because short-term studies are numerous and routine in nature, representative studies from this test type are audited quarterly to ensure the studies are designed and conducted in compliance with the Good Laboratory Practice Standards.

Reported by: William J. Lynam 9/22/87

William J. Lynam
Quality Assurance Auditor

Date

GENERAL INFORMATION

Material Tested: Propanenitrile, 2-amino-2-methyl-

Medical Research No.: 8165-001

Haskell No.: 16,716

Physical Form: Brown liquid

Purity: 68.1%

Composition: The following composition data was determined from analyses by W. M. Coleman, W. R. Grace and Co., 4/14/87, and from the DuPont Material Safety Data Sheet, 7/10/86:

68.1%	2-Amino-2-methylpropanenitrile	
9.0%	Ammonia	7664-41-7
2.8%	Acetone	67-64-1
0.2%	Triethylamine	121-44-8
<2%	Ammonium cyanide salt	

Synonyms:
- Vazo® 64AN
- Aminoisobutyronitrile
- AAN

Other Code: W. R. Grace and Co., Organic Chemicals Division, PP777-08.

CAS Registry No.: 19355-69-2

One-hour Inhalation Median Lethal Concentration (LC50) Study of Vazo® 64AN in Rats

SUMMARY

Groups of 5 male and 5 female Crl:CD®BR rats were each exposed for 1 hour to Vazo® 64AN vapor in air. The test atmospheres contained vapors of aminonitrile (active ingredient; 68.1% component), ammonia and other minor components of the test material. Following exposure, rats were weighed and observed for 14 days of recovery.

No deaths occurred following exposure to 109 ppm of aminonitrile. In contrast, several deaths occurred following exposure to 113 ppm and above. All deaths occurred during exposure. Rats that survived exposure to Vazo® 64AN had no significant adverse signs of toxicity during the recovery period.

Under the conditions of this test, 1-hour inhalation LC50's for the active ingredient of Vazo® 64AN could not be calculated due to the steep dose-response curve observed. However, 1-hour LC50's for male rats, female rats, and both sexes combined were estimated to be 111, 114 and 112 ppm, respectively. The ammonia concentrations present in the test atmospheres were not considered in the LC50 calculations because the observed ammonia concentrations were well below those expected to cause death. Based on the aminonitrile concentrations that caused death, this material is considered highly toxic on an acute inhalation basis.

Work by: Clarence W. Hutt III 9/22/87
Clarence W. Hutt, III
Technician

Study Director: Laura A. Kinney 9/22/87
Laura A. Kinney
Chemist

Approved by: NCChromey 9/28/87
Nancy C. Chromey, Ph.D.
Section Supervisor
Acute and Developmental Toxicology Section

LAK:smk:HLR69.10

INTRODUCTION

The purpose of this study was to determine a 1-hour inhalation median lethal concentration (LC50) for Vazo® 64AN in male and female rats. The LC50 was defined as the calculated atmospheric concentration of test material expected to cause the death of 50% of exposed rats either on the day of exposure or within 14 days post exposure. The procedures used were generally in accordance with the recommended testing procedures of the Department of Transportation, 49 CFR Parts 172 and 173, Packaging and Placarding Requirements for Liquids Toxic by Inhalation (1).

MATERIALS AND METHODS

A. Animal Husbandry

Young adult male and female Crl:CD®BR rats were received from Charles River Breeding Laboratories, Kingston, New York. Each rat was assigned a unique 6-digit identification number which corresponded to a numbered card affixed to the cage. Rats were quarantined for at least one week prior to testing, and were weighed and observed at least once per week during the quarantine period. During the test, rats were housed in pairs in 8" x 14" x 8" suspended, stainless steel, wire-mesh cages. The rat assigned the lower number in each cage was identified by a slash in the right ear. Prior to exposure, rats' tails and cage cards were color-coded with water-insoluble markers so that individual rats could be identified after exposure. Male rats were 8 weeks old and weighed between 233 to 279 grams on the day of exposure. Female rats were 9 to 11 weeks old and weighed between 172 and 251 grams on the day of exposure. Except during exposure, Purina Certified Rodent Chow® #5002 and water were available *ad libitum*.

B. Exposure Protocol

Groups of 5 male and 5 female rats were used for each exposure. Each rat was individually restrained in a perforated, stainless steel cylinder with a conical nose piece. The restrainers were inserted into a face plate on the exposure chamber such that only the nose of each rat protruded into the chamber. Each group was exposed nose-only for 1 hour to a vapor atmosphere of Vazo® 64AN in air. Rats were weighed prior to exposure, and were observed for clinical signs of toxicity during exposure and when released from restrainers after exposure. Surviving rats were weighed and observed daily for 14 days post exposure, weekends and holidays excluded.

C. Atmosphere Generation

Vapor atmospheres of Vazo® 64AN were generated by pumping small droplets of the liquid test material into a 3-neck round bottom glass mixing flask (500 mL) heated to between 34-43°C. The liquid test material was cooled during generation to prevent uncontrolled evaporation. Air introduced at the flask (approximately 52 L/min) swept the resulting vapors through a dispersion funnel and into the 38-liter cylindrical glass exposure chamber. The outer surface of the chamber was cooled with X-Cold® bricks during exposure to help control the chamber temperature. The chamber exhaust was drawn through a scrubber containing acetone, a dry ice cold trap and a MSA cartridge filter prior to being discharged into the hood.

D. Analytical

Two analytical methods were used to measure the atmospheric concentration of Vazo® 64AN. During each exposure, a gas chromatographic analysis was used to measure the atmospheric concentration of aminonitrile vapor (active ingredient). During most exposures, a colorimetric method was used to estimate the atmospheric concentration of ammonia. The purpose of the colorimetric analysis was mainly to monitor the relative proportions of ammonia and aminonitrile in the test atmospheres.

1. Aminonitrile Analysis

The atmospheric concentration of aminonitrile was determined at approximately 15-minute intervals during each exposure. Known volumes of the chamber atmosphere were drawn from the rats' breathing zone through 2 tandem midget impingers containing acetonitrile as a trapping solvent. The resulting solutions were analyzed in duplicate with a Hewlett Packard Model 5890A gas chromatograph equipped with a flame ionization detector. Samples were chromatographed isothermally at 50°C on a 10 m x 0.53 mm megabore column coated with dimethylpolysiloxane (2.65 micron film thickness). The atmospheric concentration of aminonitrile was calculated by comparing peak areas with standard curves prepared daily. Standards were prepared as needed by diluting known amounts of liquid Vazo® 64AN in acetonitrile.

2. Ammonia Analysis

Principle of Method: The aminonitrile in the Vazo® 64AN mixture is known to rapidly decompose to form ammonia (1:1 ratio) in the presence of water. Therefore, the ammonia content of chamber samples collected in water is a reflection of both the atmospheric ammonia and the atmospheric aminonitrile concentrations. Water samples were collected from the test atmosphere and were analyzed by the Phenate Method (2) for ammonia. With this method, indophenol (an intensely blue compound) is formed by the

reaction of ammonia or primary amines with hypochlorite and phenol. The reaction is catalyzed by a manganous salt. The color intensity of the resulting solutions is analyzed spectophotometrically to determine ammonia content. The difference between the total ammonia concentration determined by this method and the aminonitrile concentration determined by the GC method was used to estimate the atmospheric concentration of ammonia.

Reagents: Hypochlorous acid reagent was prepared weekly by adding 10 mL of 5% commercial bleach (Clorox®, 5.25% sodium hypochlorite) to 40 mL distilled, deionized water. The pH was adjusted to between 6.5 to 7.0 with concentrated hydrochloric acid using a Beckman® 4500 Digital pH meter. Manganous sulfate solution was prepared by dissolving approximately 50 mg manganous sulfate monohydrate in 100 mL distilled, deionized water. Phenate reagent was prepared weekly by dissolving approximately 2.5 g sodium hydroxide and 10 g phenol in 100 mL distilled, deionized water.

Standards and Sampling Procedure: During most exposures, samples of the chamber atmosphere were collected at approximately 30-minute intervals by drawing known volumes of the chamber atmosphere through 2 tandem midget impingers containing distilled, deionized water. The resulting solutions were diluted 1/20 in distilled, deionized water. A stock ammonia standard was prepared as needed by dissolving a known amount of anhydrous ammonium chloride (predried at 100°C for at least 1 hour) in distilled, deionized water. The stock standard was diluted to 3 standard concentrations daily.

Treatment and Analysis of Solutions: A blank solution of distilled, deionized water, 3 standard solutions and the chamber samples were treated simultaneously. A 10 mL aliquot of each solution was pipetted into a 50 mL beaker. One drop of manganous sulfate solution was added, and the beakers were placed on magnetic stirrers. Hypochlorous acid solution (0.5 mL) was added, followed immediately by the dropwise addition of 0.6 mL phenate reagent. The solutions were then stirred for approximately 15-30 minutes. The absorbance of the resulting solutions was measured with a Bausch and Lomb Spectronic® 2000 dual-beam spectrophotometer (wavelength - 630 nm, pathlength - 1 cm). The spectrophotometer was zeroed with the blank water solution. The total concentration of ammonia and aminonitrile in the test atmosphere was determined by comparing the absorbance of the chamber water samples to standard curves. The atmospheric concentration of ammonia was estimated from the difference between the average total concentration determined by the spectrophotometric method and the mean aminonitrile concentration determined by the gas chromatographic analysis.

E. Records Retention

All raw data and the final report will be stored in the archives of Haskell Laboratory for Toxicology and Industrial Medicine, Newark, Delaware, or in the DuPont Records Management Center, E. I. du Pont de Nemours and Company, Inc., Wilmington, Delaware.

RESULTS

A. Exposure Conditions and Rat Mortality

Chamber temperature ranged between 26-29°C, relative humidity ranged from 10-12%, and chamber oxygen content was 21%. The atmospheric concentrations of aminonitrile and ammonia and rat mortality data for each exposure are summarized in the following table.

Atmospheric Concentrations of Aminonitrile and Ammonia in the Vazo® 64AN Atmospheres and Rat Mortality

Aminonitrile[a] Concentration (ppm)			Estimated[b] Ammonia Concentration (%)[c]	Mortality (# deaths/#exposed)	
Mean	S.D.	Range		Males	Females
109	2.71	105 - 111	85 ppm (78%)	0/5	0/5
113	5.47	107 - 120	d	5/5	5/5
122	6.13	116 - 127	89 ppm (73%)	5/5	3/5
141	3.12	137 - 145	107 ppm (76%)	5/5	5/5

[a] Concentration of the active ingredient in the Vazo® 64AN formulation as determined by gas chromatographic analysis.

[b] Estimated ammonia concentration (calculated from the difference between the average total concentration (ammonia and aminonitrile) determined colorimetrically and the mean aminonitrile concentration determined chromatographically).

[c] Percent ammonia in the test atmosphere relative to aminonitrile. Based on the molar composition of the liquid test material, the ammonia concentration should be 58% of the aminonitrile concentration.

[d] The ammonia samples for this exposure were accidently discarded prior to being analyzed.

B. Clinical Observations

During exposure, rats in all groups had a red nasal discharge. Rats exposed to concentrations of 113 ppm and above had a diminished or no response to sound. All deaths occurred during exposure. Rats exposed to 109 ppm had no adverse clinical signs immediately following exposure. The 2 female rats that survived exposure to 122 ppm were lethargic immediately following exposure. No significant weight loss or clinical signs were observed during the 14-day recovery period.

DISCUSSION

The observed ammonia concentrations were greater than expected based on the composition of the liquid formulation. However, because ammonia is much more volatile than the aminonitrile, we anticipated that some uncontrolled evaporation of ammonia may occur. Further, the method used to assess ammonia was not precise but rather provided a rough approximation of ammonia concentration.

The ammonia concentrations observed are not expected to have caused the deaths that occurred in this study. One-hour LC50's for ammonia in rats have been reported in the literature as being between 7,340 and 16,600 ppm (3,4,5). The estimated ammonia concentrations in these atmospheres were well below those expected to cause death.

One-hour LC50's for the active ingredient of Vazo® 64AN could not be calculated (6) due to the steep dose-response curve observed. However, 1-hour LC50's in male rats, female rats, and both sexes combined were estimated to be 111, 114 and 112 ppm of aminonitrile, respectively. The estimated ammonia concentrations were excluded from the LC50 calculations because the observed concentrations were well below those expected to cause death.

CONCLUSION

Under the conditions of this study, 1-hour LC50's for Vazo® 64AN active ingredient could not be calculated due to the steep dose-response curve observed. However, 1-hour LC50's for this material were estimated to be between 111 and 114 ppm. This material is considered highly toxic on an acute inhalation basis (1-hour LC50 between 40 and 400 ppm).

References:

(1) Federal Register, Vol. 50, No. 195, October 8, 1985, pp. 41092-41097.

(2) Standard Methods for the Examination of Water and Wastewater, 14th Edition, 1975, pp. 416-417.

(3) Appelman, L. M., et. al. Am. Ind. Hyg. Assoc. J. 43(9):662-665 (1982).

(4) Prokup'eva, A. S., et. al. Gig. Tr. Prof. Zabol. 17(6):56-57 (1973); (CA 79:74521y).

(5) Vernot, E. H., et. al. Tox. Appl. Pharm. 42:417-423 (1977).

(6) LC50 calculated by the method of Finney, D. J., Probit Analysis, 3rd Edition, Cambridge University Press (1971).

Triage of 8(e) Submissions

Date sent to triage: 2/5/96

NON-CAP CAP

Submission number: 13171 A

TSCA Inventory: Y N D

Study type (circle appropriate):

Group 1 - Dick Clements (1 copy total)

ECO AQUATO

Group 2 - Ernie Falke (1 copy total)

ATOX SBTOX SEN w/NEUR

Group 3 - Elizabeth Margosches (1 copy each)

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STOX/ONCO CTOX/ONCO IMMUNO CYTO NEUR

Other (FATE, EXPO, MET, etc.): _____

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CECATS DATA:
Submission # 8EHQ-0992-13171 SEQ. A

TYPE: (INT.) SUPP FLWP

SUBMITTER NAME: E. I. Dupont de Nemours and Company

SUB. DATE: 09/11/92 OTS DATE: 09/22/92 CSRAD DATE: 03/24/95

INFORMATION REQUESTED: FLWP DATE:
0501 NO INFO REQUESTED
0502 INFO REQUESTED (TECH)
0503 INFO REQUESTED (VOL ACTIONS)
0504 INFO REQUESTED (REPORTING RATIONALE)

DISPOSITION:
(0676) REFER TO CHEMICAL SCREENING
0678 CAP NOTICE

VOLUNTARY ACTIONS:
(0401) NO ACTION REPORTED
0402 STUDIES PLANNED/UNDERWAY
0403 NOTIFICATION OF WORKER PROTECTION
0404 LABEL/MSDS CHANGES
0405 PROCESS/HANDLING CHANGES
0406 APP/USE DISCONTINUED
0407 PRODUCTION DISCONTINUED
0408 CONFIDENTIAL

CHEMICAL NAME:
VAZO 64AN
Ammonia
Acetone

CAS#
19355-69-2
7664-41-7
67-64-1

121-44-8 Triethylamine
misc. chemicals → none
ammonium cyanide salt → unknown

INFORMATION TYPE:		P F C
0201	ONCO (HUMAN)	01 02 04
0202	ONCO (ANIMAL)	01 02 04
0203	CELL. TRANS (IN VITRO)	01 02 04
0204	MUTA (IN VITRO)	01 02 04
0205	MUTA (IN VIVO)	01 02 04
0206	REPRO/TERATO (HUMAN)	01 02 04
0207	REPRO/TERATO (ANIMAL)	01 02 04
0208	NEURO (HUMAN)	01 02 04
0209	NEURO (ANIMAL)	01 02 04
0210	ACUTE TOX. (HUMAN)	01 02 04
0211	CHR. TOX. (HUMAN)	01 02 04
(0212)	ACUTE TOX. (ANIMAL)	01 02 04
0213	SUB ACUTE TOX (ANIMAL)	01 02 04
0214	SUB CHRONIC TOX (ANIMAL)	01 02 04
0215	CHRONIC TOX (ANIMAL)	01 02 04

INFORMATION TYPE:		P F C
0216	EPI/CLIN	01 02 04
0217	HUMAN EXPOS (PROD CONTAM)	01 02 04
0218	HUMAN EXPOS (ACCIDENTAL)	01 02 04
0219	HUMAN EXPOS (MONITORING)	01 02 04
0220	ECO/AQUA TOX	01 02 04
0221	ENV. OCCC/REL/FATE	01 02 04
0222	EMER INCI OF ENV CONTAM	01 02 04
0223	RESPONSE REQEST DELAY	01 02 04
(0224)	PROD/COMP/CHEM ID	01 02 04
0225	REPORTING RATIONALE	01 02 04
0226	CONFIDENTIAL	01 02 04
0227	ALLERG (HUMAN)	01 02 04
0228	ALLERG (ANIMAL)	01 02 04
0239	METAB/PHARMACO (ANIMAL)	01 02 04
0240	METAB/PHARMACO (HUMAN)	01 02 04

INFORMATION TYPE:		P F C
0241	IMMUNO (ANIMAL)	01 02 04
0242	IMMUNO (HUMAN)	01 02 04
(0243)	CHEM/PHYS PROP	01 02 04
0244	CLASTO (IN VITRO)	01 02 04
0245	CLASTO (ANIMAL)	01 02 04
0246	CLASTO (HUMAN)	01 02 04
0247	DNA DAM/REPAIR	01 02 04
0248	PROD/USE/PROC	01 02 04
0251	MSDS	01 02 04
0299	OTHER	01 02 04

TRIAGE DATA:

NON-CBI INVENTORY
(YES)
CAS SR
NO
IN TRANSIT

ONGOING REVIEW
YES (DROP/REFER)
NO (CONTINUE)
REFER

SPECIES
RAT

TOXICOLOGICAL CONCERN:
LOW
MED
(HIGH)

USE:

PRODUCTION:

COMMENTS

13171A

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Acute inhalation toxicity in rats is of high concern. Single 1-hour inhalation exposures to Crl:CD BR rats (5/sex/group) at levels of 109, 113, 122, and 141 ppm (active ingredient) were lethal (0/10, 10/10, 8/10, and 10/10, respectively). The LC_{50} could not be calculated due to the steep dose-response curve, but it was estimated to be 112 ppm. During exposure all rats had red nasal discharge, and rats exposed to ≥113 ppm had diminished or no response to sound. The two 122-ppm females that survived were lethargic immediately post-exposure.